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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
CANELLA,K	
ART UNIT	**PAPER NUMBER**
1642	32

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/862,442	Shyjan
Examiner	**Art Unit**
Karen Canella	1642

-- Th MAILING DATE of this communication appears on the cov r she t with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *29, 31-38, 43, and 45-56* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *29, 31-38, 43, and 45-56* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Response to Amendment

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

2. Claim 35 has been amended. Claims 29, 31-38, 43 and 45-56 are under consideration.

New Claim Rejections

3. Claims 29, 31-38, 43 and 45-56 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility. The claims are drawn to the polypeptide encoded by the polynucleotides of the fomy030 and fohy030 genes as represented as SEQ ID NO:3, 7 and 9. The specification teaches that the polynucleotides of SEQ ID NO:2, 6, and 8 are downregulated in metastatic cancer cells. The specification does not teach that the polynucleotide sequences of SEQ ID NO:2, 6 and 8 are actually translated into protein which is expressed in any disease state. Although the specification teaches that the fomy030 and fohy030 mRNA is expressed in proliferating non-metastatic tissue in contrast to metastatic cells there is no objective evidence that SEQ ID NO:2, 6 and 8 are translated to SEQ ID NO:3, 7 and 9. Those of skill in the art, recognize that expression of mRNA does not dictate the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the transnational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp.2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with

levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, predictability of protein translation is not necessarily contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Therefore, one of skill in the art would not be able to predict if SEQ ID NO:2, 6 and 8 were in fact translated into the polypeptides of SEQ ID NO:3, 7 and 9. Furthermore, claims 43, 45, 46, 47, 51, 52 and 53 are drawn in part to an isolated polypeptide encoded by a nucleic acid which hybridizes to SEQ ID NO:2, 6 and 8. The specification teaches the putative fomy030 and fohy030 as SEQ ID NO:3, 7 and 9 are the predicted amino acid sequence encoded from SEQ ID NO:2, 6 and 8. The specification does not suggest a protein which would be encoded from a polynucleotide which hybridizes to SEQ ID NO:2, 6 and 8. The teachings in the specification are an invitation to experiment wherein the artisan is invited to elaborate a functional use for a putative polypeptide. Because the claimed invention is not supported by a specific substantial asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

4. Claims 29, 31-38, 43 and 45-56 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

5. In the event that Applicants might be able to overcome the 35 USC 101 rejection above, the specification would still be enabling only for claims limited to full length SEQ ID NO:3, 7 and 9, or to isolated polypeptides encoded by the cDNA of the deposited clones, or the full length SEQ ID NO:2, 6 and 8 as the specification does not reasonably provide enablement for fragments of SEQ ID NO:3, 7, or 9 or isolated polypeptides encoded by polynucleotides which hybridize under stringent conditions to the cDNA of the deposited clones of NRLL No. B21426, ATCC No. 97880 or ATCC No. 97881; or the isolated polypeptide encoded by polynucleotides which hybridize under stringent conditions to SEQ ID NO:2, 6, 8 or the complement of SEQ ID NO:2, 6 or 8; or isolated polypeptides encoded by polynucleotides that comprise at least 30 nucleotides

which hybridize under stringent conditions to SEQ ID NO:2, 6, 8, the complement of SEQ ID NO:2, 6 or 8, or the cDNA of the deposited clones of NRLL No. B21426, ATCC No. 97880 or ATCC No. 97881. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

(A)As drawn to polypeptides encoded by polynucleotides which hybridize to disclosed sequences.

Claims 43 and 45-56 encompass polynucleotides comprising non-disclosed nucleic acid sequences attached to polynucleotides that encode SEQ ID NO:3, 7 and 9, that is polynucleotides that hybridize to said polynucleotides under stringent conditions and are complementary to said polynucleotides The recitation of stringent hybridization conditions is not limiting. As disclosed above, the specification does not teach how to use the polypeptides encoded by SEQ ID NO:2, 6 or 8. Clearly, since the specification has not taught how to use said polynucleotides, the specification has not enabled the scope of claims drawn to polypeptides encoded by polynucleotides that hybridize to SEQ ID NO:2, 6 or 8 or the cDNAs contained in the deposited clones. When given the broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species including cDNA and mRNA species having variant sequences from the polynucleotides of SEQ ID NO:2, 6 and 8 and the function of the proteins encoded by these variant polynucleotides cannot be anticipated as protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, as disclosed by Burgess et al (J of Cell Bio. 111:2129-2138, 1990), replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. (Lazar et al, Molecular and Cellular Biology, 1988, Vol. 8:1247-1252). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Clearly, it could not be predicted that a polynucleotide comprising 30 nucleotides which

hybridizes to SEQ ID NO:2, 6 or 8 would even encode a member of the 030 family or that a protein that is encoded by a variant of SEQ ID NO:2, 6 or 8 will function as suggested and the specification fails to provide an enabling disclosure for said polypeptides. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use the polypeptides encoded by the polynucleotide variants thereof, In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

(B)As drawn to polypeptides comprising a partial amino acid sequence of SEQ ID NO:7 and SEQ ID NO:9.

Claims 37 and 38 are drawn to polypeptides comprising part of the sequences of SEQ ID NO:7. The specification teaches that the putative fohy030 comprises the amino acid sequence of SEQ ID NO:7. The specification teaches that the hypothetical sequences of SEQ ID NO:7 and 9 are similar in the two regions represented by amino acids 1-844 and 850-1497 of SEQ ID NO:7. For the reasons given in the rejections of paragraphs 3 and 4 supra, the specification is not enabling for the isolated polypeptides of SEQ ID NO:7 and 9. Further, the specification does not suggest a function associated with an isolated fragment of SEQ ID NO:7 consisting of residues 1-844 or residues 850-1497 of SEQ ID NO:7 or a protein comprising one of amino acid residues 1-844 or 850-1497 of SEQ ID NO:7.. The specification does not teach that amino acid residues 1-844 and 850-1497 of SEQ ID NO:7 would retain the activity or expression pattern of fohy030 when inserted separately into different proteins.. Further, the specification does not demonstrate that insertion of amino acid residues 1-850 of SEQ ID NO:7 into a different amino acid context would result in a fohy030 protein. For example it is well known in the art that proteins are folded 3-dimensional structures, the function and stability of which are directly related to a specific conformation (Mathews and Van Holde, Biochemistry, 1996, pp. 165-171). In any given protein, amino acids distant from one another in the primary sequence may be closely located in the folded, 3-dimensional structure (Mathews and Van Holde, Biochemistry, 1996, pp. 166, figure 6.1). The specific conformation of a protein results from non-covalent interactions between amino acids, beyond what is dictated by the primary amino acid sequence. A different amino acid

sequence surrounding a fragment of SEQ ID NO:7 can potentially radically alter the three dimensional structural environment in which the given fragment is located (Matthews, B. "Genetic and Structural Analysis of the Protein Stability Problem") thus, the consequences of the altered sequence environment cannot be predicted. Additionally, it is recognized in the art that protein function is context dependent, and cellular aspects, such as membrane anchorage, protein activation and sub-cellular location must be considered with respect to protein function in addition to molecular aspects, (Bork, P., Genome Research, 2000, Vol. 10, pp.398-400 especially p. 398, col 2). Due to these reasons, one of skill in the art would be forced into undue experimentation in order to practice the invention as claimed.

Claim Rejections Maintained

6. The rejection of claims 37, 38, 43 and 45-56 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is maintained. Applicant argues that the instant specification contemplates the variant polypeptides as being encoded by the variant polynucleotides which hybridize to the disclosed polynucleotides, or as being recombinantly expressed as truncated fusion proteins. This was not found persuasive as the specification did not provide any objective evidence that applicant had the variant polypeptides in hand at the time the instant application was filed. The written description in this case only sets forth the putative SEQ ID NO:3, 7 and 9 assumed to be encoded by SEQ ID NO:2, 6 and 8 or equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to polypeptides comprising amino acid residues 1-844 of SEQ ID NO:7, amino acids 850-1497 of SEQ ID NO:7, polypeptides encoded by polynucleotides which hybridize to the disclosed gene sequences of fomy030 and fohy030.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry,

whatever is now claimed. (See page 1117). The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO:3, 7 and 9, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides for the reasons given in the rejection of paragraph 5 above, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Furthermore, In The Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that an adequate written description of a DNA requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention. However, no disclosure, beyond the mere mention of variant polypeptides encoded by variant polynucleotides is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated polypeptides of SEQ ID NO:3, 7 and 9, or isolated polypeptides encoded by SEQ ID NO:2, 6 and 8, or the cDNA of the deposited clones of NRRL deposit No. B-21416, or ATCC No. 97880 and 97881, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

7. All other rejections and objections as stated in Paper No. 27 are withdrawn.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Patent Examiner, Group 1642
April 22, 2001

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